



## **BEYOND PESTICIDES**

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April 6, 2009

Office of Pesticide Programs (OPP)  
Regulatory Public Docket (7502P),  
Environmental Protection Agency,  
1200 Pennsylvania Ave., NW.,  
Washington, DC 20460-0001

**Re: Data Requirements for Antimicrobial Pesticides. Docket Number: EPA-HQ-OPP-2008-0110**

Dear Sir/Madam:

Beyond Pesticides appreciates the opportunity to comment on the Proposed Rule; Data Requirements for Antimicrobial Pesticides. The U.S. Environmental Protection Agency (EPA), with these new rules, proposes to revise and update the existing data requirements for antimicrobial pesticides. Currently, the agency does not have a separate listing of data requirements for antimicrobial pesticides. Often the agency would conduct case-by-case determinations to instruct registrants on what data was needed for submission. However, this invariably led to inconsistencies among data submissions and data gaps, which continue to plague the agency's review processes. Due to the unique use patterns of antimicrobial pesticides, it is necessary to establish a separate set of data requirements for all antimicrobial so that the process is uniform, efficient and reduces uncertainties.

We applaud EPA's decision to go forward with these new rules and support the new revisions and inclusion of nine new data requirements. We also appreciate the agency's recognition that many antimicrobial pesticides are indeed washed down the drain and discharged into wastewater treatment plants (WWTPs). With this, we support EPA's incorporation of modeling techniques, e.g. the Down the Drain Model, to assist in the evaluation of the environmental fate and impact of antimicrobials, their impact on WWTP processes, and the long-term improvement of the agency's hazard analyses.

These new rules are a step in the right direction when it comes to the impact of antimicrobials on human and environmental health. We believe they are indeed necessary considering the proliferation of these substances in the consumer marketplace. There are a few suggestions that we would like the agency to consider as it moves forward with finalizing these new rules:

## Indirect Food Use of Antimicrobials

More attention is needed for the indirect contamination of food by antimicrobial substances. Many surfaces and packaging materials have been impregnated with antimicrobial agents, such as silver nanoparticles and triclosan. These substances, and/or their degradates, have the ability to migrate from these surfaces and onto food, resulting in indirect dietary exposures. The nation's surface waters are also contaminated with high concentrations of antimicrobial compounds.<sup>1,2</sup> This means that not only is drinking water contaminated, but fish and other aquatic organisms that are ingested by humans. Under the Federal Food, Drug and Cosmetic Act (FFDCA), the EPA is mandated to determine that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information. *FFDCA, Sec. 408(b)(2)(A)(ii).*

The agency has proposed to delineate between high and low indirect food use exposures. Low exposures are to be defined as those which result in residues in or on food of less than 200 ppb. It is not apparent whether the agency recognizes that continual exposure to "low exposure residues" over the long-term results in high exposure. Continual low dose exposure has been shown in the scientific literature to pose significant long term risk, especially for developing infants.<sup>3</sup> According to the Federal Registrar Notice,<sup>4</sup> the EPA once considered all food use antimicrobials high exposure. We suggest that all uses, whether direct or indirect food uses, be considered high exposure instead of delineating between high and low exposures. This should be the case since the agency has defined high exposure as "that resulting in human exposures over a considerable portion of the human lifespan," such as (but not limited to) food and water exposures.<sup>4</sup>

## SAR and QSAR

EPA proposes to utilize structure activity relationships (SAR) and quantitative structure activity relationship (QSAR) modeling to assist in the fulfillment of data requirements for antimicrobials. These techniques involve the comparison of the molecular structure of chemicals to that of other structurally-related chemicals for which data are available. These structural similarities can be used to make predictions about the physical, chemical and/or biological activity of the chemical being assessed. The use of these practices could potentially conserve resources, increase efficacy and provide information for a chemical with otherwise limited data. The use of SARs and QSARs should be a supplement to data submitted and should by no means be a substitute for available, reliable, measured data (laboratory studies).

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<sup>1</sup> Halden, R.U., and Paull, D.H. 2005. Co-occurrence of triclocarban and triclosan in US water resources. *Environmental Science & Technology* 39, 1420-1426.

<sup>2</sup> Kolpin, D.W., E.T. Furlong, M.T. Meyer, E.M. Thurman, et al. 2002. Pharmaceuticals, Hormones, and other organic wastewater contaminants in U. S. streams, 1999-2000: A national reconnaissance. *Environ. Sci. Technol.* 36, 1202-1211.

<sup>3</sup> Lassiter et al. 2008. Exposure of Neonatal Rats to Parathion Elicits Sex-Selective Reprogramming of Metabolism and Alters the Response to a High-Fat Diet in Adulthood. *Environ. Health Perspectives.* 116(11); Lu et al. 2008. Dietary Intake and Its Contribution to Longitudinal Organophosphorus Pesticide Exposure in Urban/Suburban Children. *Environ. Health Perspectives.* 116 (4)

<sup>4</sup> U.S. EPA. 2008. Data Requirements for Antimicrobial Pesticides; Proposed Rule. Federal Registrar, Vol. 73, No. 196, October 8, 2008.

The agency has a history of utilizing SARs, however, it has been usually on a case-by-case basis and generally sporadic. It has been our experience that the agency chooses to utilize SARs when it is convenient to do so, and ignores them in other cases if the weight against the use of the chemical were to increase. We hope that the agency would be consistent in its use of SARs, even when done on a case-by-case basis. We also recommend that the use of SARs be used to predict modes of action of chemicals, as they relate to common mechanisms of toxicity. The agency has a tendency to recognize structural similarities between chemicals while dismissing the potential of having similar modes of action, despite scientific evidence demonstrating similar adverse impacts/endpoints for pesticidal substances with structural similarities. (Please refer to Beyond Pesticides' previous comments for the preliminary RED for triclosan and the petition to ban 2,4-D.)

### **Down the Drain Model**

This model proposed by the agency to estimate concentrations of chemicals in surface waters, as a result of disposal of consumer products into wastewaters, is a useful tool to assist wastewater treatment agencies with the wastewater treatment process, and to monitor the fate and effects of these chemicals once in the waterways. This, along with the new environmental fate studies to identify potential harm to the microbial treatment processes at WWTPs, would provide data on the fate and effects of these chemicals in sewage sludge. This is important since sewage sludge is often recycled on agricultural lands and can potentially contaminate the food supply.

We recommend that when using the model, the agency also takes into account transformation and degradation products of the antimicrobial substances under review, and their impacts on surface waters, microbial communities in WWTPs, as well as in sewage sludge. For example, a study investigating triclosan in WWTPs found that high concentrations of its metabolite methyl triclosan were found to be emitted from the plants as a result of biological methylation of triclosan occurring within the plants.<sup>5</sup> Methyl triclosan is however, much more persistent and bio-accumulative than its parent.

### **Other Issues of Concern**

We also recommend that the agency take a closer look at chemical mixtures currently found in the nation's waterways and their possible synergistic effects. Several studies exist that detail the presence of varied concentrations of pharmaceuticals in surface waters, including several antimicrobials.<sup>6</sup> However, little to no effort has been made toward investigating how these

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<sup>5</sup> Balmer, M.E., T. Poiger, C. Droz, K. Romanin et al. 2004. *Occurrence of methyl triclosan, a transformation product of the bactericide triclosan, in fish from various lakes in Switzerland*. Environmental Science and Technology 2004. 38: p. 390-395

<sup>6</sup> Kolpin, D.W., E.T. Furlong, M.T. Meyer, E.M. Thurman, et al. 2002. Pharmaceuticals, Hormones, and other organic wastewater contaminants in U. S. streams, 1999-2000: A National Reconnaissance. Environ. Sci. Technol. 36, 1202-1211.

chemicals interact with each other in the environment, or their combined effects on human and environmental health. Recent studies have found that mixtures of pesticides in surface water, especially at low doses, have a dramatic adverse impact on aquatic species compared to the individual chemical.<sup>7</sup> The agency cannot rule out that antimicrobial mixtures occurring in the environment have an added impact on environmental health. As such, the agency must allocate resources to look at this phenomenon which has so far been ignored in risk analyses.

The widespread and indiscriminate use of antimicrobial agents can lead to the development of resistant bacteria. Several peer-reviewed studies have been previously submitted to the agency detailing this prospect. It has also been brought to the agency's attention that cross resistance to antibiotics may also be a consequence of widespread antimicrobial use. While the EPA maintains that it continues to work with the Interagency Task Force on Antimicrobial Resistance and will monitor the issue, we feel that this is inadequate given the gravity of the consequences that resistant bacteria can pose to human health, especially to vulnerable populations including infants and children, the elderly and the immuno-compromised. Knowing that for most antimicrobial substances the EPA oversees there is no efficacy data, and that most of these are ineffective and unnecessary, we believe the agency must find that for these substances, the risks far outweigh any perceived benefit.

## **Conclusion**

Beyond Pesticides believes that these rules are long overdue and are necessary if the agency is serious about protecting human and environmental health from the impacts of antimicrobials. Antimicrobial substances have exploded onto the consumer market place with little to no regulatory oversight and little to no data on their fate and effect in the environment. These rules will help to ensure that additional scrutiny is placed upon these chemicals and that the risk assessment process is strengthened.

We hope that these new requirements will also help to close many of the outstanding data gaps that plague the risk assessment process of many chemicals under the EPA's jurisdiction. The agency must move expeditiously to establish these new requirements so as to ensure that antimicrobial substances do not pose unreasonable hazards to human and environmental health.

As the agency moves forward, these new requirements must be implemented in a context that enables EPA to take restrictive action in the face of incomplete and inadequate data. Since

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<sup>7</sup> Relyea, RA. 2009. A cocktail of contaminants: how mixtures of pesticides at low concentrations affect aquatic communities. *Oecologia*. 159(2):363-76; Laetz, C,A et al. 2009. The Synergistic Toxicity of Pesticide Mixtures: Implications for Risk Assessment and the Conservation of Endangered Pacific Salmon. *Environ. Health Perspec.* 117 (3); Tierney et al. 2008. Salmon Olfaction is Impaired by an Environmentally Realistic Pesticide Mixture. *Environ. Sci. Technol.* 42 (13): 4996–5001

widespread exposure to antimicrobials through contaminated water, aquatic life, sludge and food exposes human and environmental health to unknown and unstudied risks, urgent and restrictive action is needed now to prevent the further release of antimicrobial substances into the environment.

Thank you for your attention to our comments.

Respectfully,

Jay Feldman  
Executive Director  
Beyond Pesticides

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Beyond Pesticides